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TRANSMITTAL FORM (to be used for all correspondence after initial filing)	Application Number	10/617,979
	Filing Date	July 11, 2003
	First Named Inventor	Henkin et al
	Art Unit	Unknown
	Examiner Name	Unknown
Total Number of Pages in This Submission	Attorney Docket Number	22727/04130

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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of: Henkin et al.)	Examiner:
)	
Serial No.: 10/617,979)	Art Unit:
)	
Filed: July 11, 2003)	
)	
For: IN VITRO TRANSCRIPTION ASSAY)	
FOR T BOX ANTITERMINATION)	
SYSTEM)	
)	
Attorney Docket No.: 22727/04130)	

INFORMATION DISCLOSURE STATEMENT

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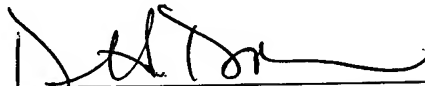
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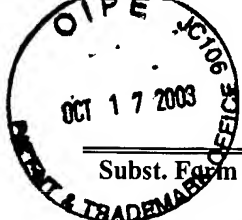
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This Information Disclosure Statement is being filed within three months of the filing of the subject application and/or prior to an Office Action. Accordingly, it is not believed that any fee is required relating to the filing of this Information Disclosure Statement. If this is not the case, the Patent Office is hereby authorized to charge any related fee to Deposit Account No. 03-0172.

Respectfully submitted,

By: 
Diane H. Dobrea (Reg. No. 48,578)
(216) 622-8485



Subst. Form PTO-1449 APPLICANT'S INFORMATION DISCLOSURE STATEMENT	Atty. Docket No.: 22727/04130	Serial No.: 10/617,979
	Applicant: Henkin, et al.	
	Filing Date: July 11, 2003	Group:

U.S. PATENT DOCUMENTS

Initial*		Document No.	Date	Name	Class	Subcl.	Filing Date
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FOREIGN PATENT DOCUMENTS

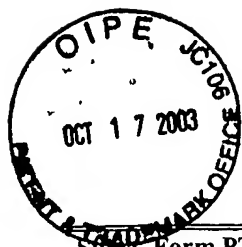
		Document No.	Date	Country	Class	Subcl.	Translation?
	AE						
	AF						
	AG						
	AH						
	AI						

OTHER PRIOR ART

	AJ	Grundy, et al., "The T box and S box transcription termination systems", The Ohio State University, 1 page.
	AK	Grundy, et al., "tRNA-mediated transcription antitermination <i>in vitro</i> : Codon-anticodon pairing independent of the ribosome", PNAS, August 20, 2002, vol. 99, no. 17, pp. 11121-11126.
	AL	Gerdeman, et al., "Solution Structure of the <i>Bacillus subtilis</i> T-box Antiterminator RNA: Seven Nucleotide Bulge Characterized by Stacking and Flexibility", J. Mol. Biol. (2003) 326, pp. 189-201.
	AM	Gerdeman, et al., " <i>In Vitro</i> structure-function studies of the <i>Bacillus subtilis</i> <i>tyrS</i> mRNA antiterminator: evidence for factor-independent tRNA acceptor stem binding specificity", Nucleic Acids Research, 2002, Vol. 30, No. 4, 1065-1072.
	AN	Yanofsky, "Transcription Attenuation: Once Viewed as a Novel Regulatory Strategy", Journal of Bacteriology, Jan. 2000, pp 1-8.
	AO	Gollnick et al., "Transcription attenuation", Biochimica et Biophysica Acta 1577 (2002) pp. 240-250.
	AP	Henkin, "Transcription termination control in bacteria", Current Opinion in Microbiology 2000, 3: pp. 149-153.
	AQ	Barbieri et al., "MicroCorrespondence", 1998 Blackwell Science Ltd., Molecular Microbiology, 29, pp. 661-664.
	AR	van de Guchte, et al., "Identity elements in tRNA-mediated transcription antitermination: implication of tRNA D- and T-arms in mRNA recognition", Microbiology (2001), 147, pp. 1223-1233.

Examiner:	Date Considered:
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*EXAMINER: Initial if reference considered, whether or not citation is in conformation with MPEP 609; draw line through citation if in conformance and not considered. Include copy of this form with next communication to applicant.



Subst. Form PTO-1449

Atty. Docket No.: 22727/04130

Serial No.: 10/617,979

APPLICANT'S INFORMATION
DISCLOSURE STATEMENT

Applicant: Henkin, et al.

Filing Date: July 11, 2003

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		Document No.	Date	Country	Class	Subcl.	Translation?
	AE						
	AF						
	AG						
	AH						
	AI						

OTHER PRIOR ART

	AKS	Kunst, et al., "The complete genome sequence of the Gram-positive bacterium <i>Bacillus subtilis</i> ", Nature, Vol. 390, 20 November 1997, pp. 249-256.
	AKT	Grundy, et al., "Sequence requirements for terminators and antiterminators in the T box transcription antitermination system: disparity between conservation and functional requirements", Nucleic Acids Research, 2002, Vol. 30, No. 7, pp. 1646-1655.
	ALU	Henkin, "Control of Transcription Termination in Prokaryotes," Annu. Rev. Genet. 1996, 30: pp. 35-57.
	AMV	Henkin, et al., "Regulation by transcription attenuation in bacteria: how RNA provides instructions for transcription termination/antitermination decisions", BioEssays 24: pp. 700-707.
	ANW	Grundy et al., "The <i>Staphylococcus aureus</i> <i>ileS</i> Gene, Encoding Isoleucyl-tRNA Synthetase, Is a Member of the T-Box Family", Journal of Bacteriology, June 1997, pp. 3767-3772.
	AOX	Putzer, et al., "Transfer RNA-mediated antitermination <i>in vitro</i> ", Nucleic Acids Research, 2002, Vol. 30, No. 14, pp. 3026-3033.
	ARV	Wagar, et al., "The Glycyl-tRNA Synthetase of <i>Chlamydia trachomatis</i> ", Journal of Bacteriology, Sept. 1995, pp. 5179-5185.
	AQ	
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The T box and S box transcription termination control systems.

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Expression of variety of aminoacyl-tRNA synthetase, amino acid biosynthesis and amino acid transporter genes in Gram-positive bacteria is controlled at the level of premature termination of transcription. Two different transcription termination control systems, the T box and S box systems, have been identified in our laboratory, each of which is characterized by the presence of a different set of conserved primary sequence and structural elements in the mRNA leader region of the regulated genes, upstream of the start of the coding sequence (1, 2, 3). This region includes a transcriptional terminator, readthrough of which is required for expression of the downstream genes, and a competing antiterminator, formation of which prevents termination of transcription (Fig. 1). The S box leaders also contain an additional element that competes with the antiterminator, and functions as an anti-antiterminator. Mutations that disrupt conserved sequence or structural elements in T box leaders generally result in loss of readthrough, while mutations in conserved elements in S box leaders result in high level constitutive expression, indicating that the two systems are mechanistically very different.

The T box system is used to regulate genes in multiple amino acid classes; individual genes in this group respond to the charging ratio of the cognate tRNA. For example, the model *Bacillus subtilis* *tyrS* gene, encoding tyrosyl-tRNA synthetase, is induced under conditions that result in accumulation of uncharged tyrosyl-tRNA, but does not respond to decreased charging of noncognate tRNAs (1, 2). The specificity of the response is dictated by two base-pairing interactions between the tRNA and the leader RNA: the anticodon of the tRNA pairs with a precisely placed triplet in the leader (the "specifier sequence"), and the acceptor end of the tRNA pairs with 4 nt of the internal bulge of the antiterminator. In contrast, the S box system is specific to genes involved in methionine metabolism, and all transcriptional units in this group respond in concert to limitation for methionine, although it is not yet known whether methionine acts directly as the effector (3).

We have identified over 200 T box leaders in the genomes of a variety of Gram-positive bacteria (including a number of pathogenic species), as well as isolated examples in Gram-negative organisms. The S box system is found in a smaller group of organisms; methionine genes in organisms such as *Streptococcus* and *Enterococcus* are regulated by the T box system, suggesting that the two mechanisms represent alternate solutions to a common regulatory problem. These large data sets provide new information about features that vary in particular sets of genes. Some of this variability is organism-specific, while other features of T box leaders vary according to the amino acid specificity of the leader. One interesting element is the GA motif, which is found in both T box and S box leaders (4); mutations disrupting this element in the *B. subtilis* *tyrS* gene, a T box gene, result in loss of readthrough, while mutations in this element in the *B. subtilis* *yitJ* gene, a member of the S box family, results in loss of repression by methionine. We are currently focusing on further elucidation of the mechanism of transcription termination control in both systems, and identification of additional factors that participate in these regulatory systems.

1. Grundy, F. J. and Henkin, T. M. (1993) *Cell* 74:475-482.
2. Grundy, F. J., Rollins, S. M., and Henkin, T. M. (1994) *J. Bacteriol.* 176:4518-4526.
3. Grundy, F. J. and Henkin, T. M. (1998) *Mol. Microbiol.* 30:737-749.
4. Winkler, W. C., Grundy, F. J., Murphy, B. A., and Henkin, T. M. (2001) *RNA* 7:1165-1172.

Key words: antitermination/gene regulation/tRNA/RNA structure